

- 8 -

Claims

- 1) A process for the synthesis of gabapentin comprising the preparation of 1,1-cyclohexanediactic acid monoamide, the Hofmann transposition of the same monoamide,
5 the purification of a gabapentin salt and the crystallization from organic solvent, characterized in that the preparation of the acid monoamide comprises:
- a) the amination of 1,1-cyclohexanediactic acid anhydride by reaction with aqueous NH_3 at a temperature lower than 30°C by using a NH_3 /anhydride molar ratio lower than 3;
 - b) the product precipitation through the acidification of the reaction mixture.
- 10 2) A process according to claim 1 wherein the amination of 1,1-cyclohexanediactic acid anhydride takes place by reaction with NH_3 generally utilized in aqueous solution with a concentration comprised between 25 and 35%.
- 3) A process according to claim 2 wherein the amination of 1,1-cyclohexanediactic acid anhydride takes place by reaction with ammonia in aqueous solution with a concentration
15 around 28%.
- 4) A process according to claim 1 wherein the acidification step is carried out with concentrated or gaseous hydrochloric acid.
- 5) A process according to claim 4 wherein the acidification step is carried out with aqueous hydrochloric acid with a concentration around 31%.
- 20 6) A process according to claim 1 wherein the molar ratio between ammonia and 1,1-cyclohexanediactic acid anhydride is comprised between 2.2 and 2.9.
- 7) A process according to claim 6 wherein the molar ratio between ammonia and 1,1-cyclohexanediactic acid anhydride is comprised between 2.5 and 2.7.
- 8) A process according to claim 1 wherein the amination of 1,1-cyclohexanediactic acid
25 anhydride is carried out at a temperature comprised between 10 and 25°C .
- 9) A precipitation process of 1,1-cyclohexanediactic acid monoamide comprising the acidification of an ammoniacal solution of the monoamide at a temperature comprised between 40 and 45°C until obtaining a pH around the values of 6.3-6.5, the continuation of the acidification step of the reaction mixture at the same temperature until obtaining a pH
30 around the values of 3.8-4.2 and, at last, the precipitate filtration by keeping the

- 9 -

temperature between 40 and 45°C.

10) A process according to claim 9 wherein the acidification step is carried out with concentrated or gaseous hydrochloric acid.

5 11) A process according to claim 10 wherein the acidification step is carried out with aqueous hydrochloric acid with a concentration around 31%.

12) A process according to claim 1 further comprising the transformation of 1,1-cyclohexanediactic acid into the corresponding anhydride.

13) A process according to claim 12 wherein the transformation of 1,1-cyclohexanediactic acid into the corresponding anhydride is carried out by reaction with acetic anhydride in the presence of an organic solvent.

14) A process according to claim 13 wherein the organic solvent is toluene.

15) A process for the preparation of 1,1-cyclohexanediactic acid monoamide comprising:

a) the amination of 1,1-cyclohexanediactic acid anhydride by reaction with aqueous NH_3 at a temperature lower than 30°C by using a NH_3 /anhydride molar ratio lower than 3;
b) the product precipitation through the acidification of the reaction mixture.

16) A process according to claim 15 wherein the amination of 1,1-cyclohexanediactic acid anhydride takes place by reaction with NH_3 generally utilized in aqueous solution with a concentration comprised between 25 and 35%.

20 17) A process according to claim 16 wherein the amination of 1,1-cyclohexanediactic acid anhydride takes place by reaction with ammonia in aqueous solution with a concentration around 28%.

18) A process according to claim 15 wherein the acidification step is carried out with concentrated or gaseous hydrochloric acid.

25 19) A process according to claim 18 wherein the acidification step is carried out with aqueous hydrochloric acid with a concentration around 31%.

20) A process according to claim 15 wherein the molar ratio between ammonia and 1,1-cyclohexanediactic acid anhydride is comprised between 2.2 and 2.9.

21) A process according to claim 20 wherein the molar ration between ammonia and 1,1-cyclohexanediactic acid anhydride is comprised between 2.5 and 2.7.

- 10 -

22) A process according to claim 15 wherein the amination of 1,1-cyclohexanediactic acid anhydride is carried out at a temperature comprised between 10 and 25°C.

23) A process according to claim 15 further comprising the transformation of 1,1-cyclohexanediactic acid into the corresponding anhydride.

24) A process according to claim 23 wherein the transformation of 1,1-cyclohexanediactic acid into the corresponding anhydride is carried out by reaction with acetic anhydride in the presence of an organic solvent.

25) A process according to claim 24 wherein the organic solvent is toluene.